REMARKS/ARGUMENTS

Claims 1-13 were pending in the instant application. Claims 5, 9-10, and 12-13 have been cancelled. Claims 1-4, 6-8, and 11 have been amended to more clearly point out and distinctly claim that which Applicants consider to be their invention. The amended claims 1-4, 6-8, and 11 are fully supported in the original claims and in the specification as originally filed on page 8, lines 1-5. Therefore, the amendments to claims 1-4, 6-8, and 11 do not add new matter. Applicants respectfully request that the amendments be entered.

Upon entry of the above-made amendments claims 1-4, 6-8, and 11 will be pending in the current application.

The following remarks, in conjunction with the above amendments, are believed to be fully responsive to the Office Action.

Information Disclosure Statement

Applicants note that the previous IDS omitted to supply copies of the foreign patent applications. Copies of the following are now provided:

WO 00/48625,
WO 01/89584,
WO 01/91805,
WO 02/26776,
WO 05/030265,
WO 05/030266,
WO 05/058370,
WO 05/058371.

Claim Rejections: 35 USC §101

Claim 13 stands rejected under 35 USC 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Applicants have now cancelled claim 13 therefore the objection is believed to be moot.

Claim Rejections: 35 USC §112.

Claims 1-13 stand rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Since claim 13 had already been cancelled, the objection is now directed to Claims 1-12.

Claim 1 has been amended to include the elements of previous claim 10. Previous claims 5, 9, 10, 12 and 13 have been cancelled. Amended claim 1 is now limited to a method of optical imaging of vulnerable atherosclerotic plaque of an animate subject and is based primarily on previous claim 10. The claim is no longer to optical imaging contrast agents *per se*. Hence, it can no longer be argued that the claim pertains to compounds defined only by their function. In addition, the claim scope has been limited to the preferred biological targets described in the specification at page 8 lines 1 to 5.

Applicants contend that the specification provides sufficient information for the person skilled in the art to reproduce the method of amended claim 1. The specification provides suitable optical reporters; a description of suitable optical imaging techniques (page 15 lines 1-18); plus a description of targeting molecules and methods of labelling them with optical

reporters. The person skilled in the art can either use the contrast agents described in the specification, or generate new ones. Applicants suggest that the claim scope for such an optical imaging method claim should not be limited by the possible future advent of new targeting molecules. If a person skilled in the art has available a compound with affinity for one of the targets described, then labelling such a compound with an optical reporter is taught by the present specification.

The revised claims 1-4, 6-8, and 11 are therefore believed to comply with 35 USC §112, and applicants contend that this objection should be withdrawn.

Claim Rejections: 35 USC §102

Weisleder

Previous claims 1-9 and 12 stand rejected under 35 USC 102 as being anticipated by Weissleder et al. to US 2003/0044353 (Weissleder).

Applicants point out that the method of currently amended claim 1 is based primarily on previous claim 10. That claim was not part of the Examiner's novelty objection based on Weissleder. Hence, revised claim 1 is believed to be already acknowledged by the Examiner to be novel over Weissleder. That is logical because Weissleder does not disclose the method of imaging atherosclerotic plaque of the present invention. Weissleder is, in fact, silent on atherosclerotic plaque - the Examiner acknowledges as much on page 9 of the office action (line 8).

Revised claims 2-4, 6-8 and 11 all depend on claim 1 and are believed novel over Weissleder for the same reasons.

Klaveness

Previous claims 1-3, 5-9 and 12 also stand rejected as being anticipated by Klaveness et al. to US 6610269 (Klaveness).

Similar comments to Weissleder (above) apply. Hence, applicants contend that revised claims 1-4, 6-8 and 11 are novel over Klaveness.

Chen [Circulation, 105(23), 2766-2771 (2002)]

Previous claims 1 and 3-13 also stand rejected as being anticipated by Chen et al to Circulation, 2002, Jun 11;105(23); pgs. 2766-71 (Chen).

Revised claim 1 specifies preferred biological targets. Cathepsin B is outside the scope. Hence amended claim 1 is not anticipated by Chen. The novelty rejection based on Chen should therefore be withdrawn.

Claim Rejections 35 USC § 103

Previous claims 1-13 stand rejected as being obvious over the combination of Weissleder to 2003/0044353 (Weissleder) in view of Klaveness et al. to US 2003/0170173 A (Klaveness2).

Applicants point out that the teaching of Klaveness2 is diverse. Firstly, the imaging modalities involved are extensive and not limited to optical imaging. See Klaveness2 at [003] – where MRI, X-ray, ultrasound, radio-imaging and others are described.

Secondly, Klaveness2 discloses lists of a wide range of enzymes, each associated with different disease states:

List 1 cancer at [008],

List 2 cardiovascular disease at [0089],

List 3 CNS enzymes at [0090],

List 3a Alzheimer's disease at [0091],

List 3b multiple sclerosis at [0092],

List 4 bone diseases at [0093],

List 5a virus infections at [0094],

List 5b bacterial infections at [0095],

List 5c fungal infections at [0096],

List 6 MMP substrates at [0193] following,

List 7 enzymes defective in inherited diseases [0205] – [0380].

The possible permutations of [enzyme substrate] + [imaging modality] arising from Klaveness2 are thus extensive, amounting to thousands of possibilities.

There is no specific teaching in Klaveness2 of an optical reporter specifically for use in the imaging of atherosclerotic plaque, as taught by the present claims. Since the teaching of Klaveness2 is so diverse and far-reaching, applicants contend that any combination [Weissleder] + [Klaveness2] in fact leads in a huge number of possible directions. From those extensive possibilities, applicants suggest that there is no teaching, suggestion of motivation to make only those choices which lead to the subject matter of the present claims. Klaveness2 provides no teaching on which of the wide range of imaging modalities described therein are suitable for imaging atherosclerotic plaque. In fact, Klaveness2 teaches at [0074] that MRI and nuclear imaging are preferred so teaches away from the optical methodology of the present claims.

Furthermore, applicants point out that Klaveness2 teaches, at [0193] – [0194] possible substrates for MMP. Applicants point out that revised claim 1 is limited to MMP-9, a specific metalloproteinase. Klaveness2 therefore provides no particular teaching in the direction of present amended claim 1.

The Examiner is correct that, at [0193], Klaveness2 teaches several possible substrates for "MMP" – including collagen. Thus, Klaveness2 teaches towards collagen as a possible labelled entity for imaging MMP activity in atherosclerotic plaque. The subject matter of present claim 1 is different, in that the claimed contrast agent has affinity for collagen. Thus, the contrast agent binds to collagen, because collagen is an "abnormally expressed biological target associated with vulnerable atherosclerotic plaque". The contrast agent does not comprise collagen itself, as taught by Klaveness2. The teaching in this regard is thus clearly

different from that of Klaveness2. Klaveness2 in fact teaches away from present claim 1 by teaching towards collagen itself as a suitable imaging agent. The obviousness rejection based on the combination Weissleder/Klaveness2 should therefore be withdrawn.

Claims 1-4, 6-8, and 11 are all believed to be allowable in view of the claim amendments and over the cited prior art.

Obviousness-type Double Patenting Rejection

Claims 1-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No(s). 10/573,604, 10/573/606, 10/582,679, 10/582,842, and 10/582,893. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated as allowable.

CONCLUSION

Applicants respectfully hold that the claims submitted herewith fulfill the requirements of a patentable invention and that all rejections and objections be withdrawn and claims 1-4, 6-8, and 11 be allowed.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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